

MSC-22859-1-CU

WHAT IS CLAIMED IS:

- 1 1. A method of inducing expression of at least one gene in a cell,
2 comprising the steps of:
3 contacting said cell with an transcription factor decoy oligonucleotide
4 sequence directed against a nucleotide sequence encoding a shear stress response
5 element; and
6 determining the expression of said gene in said cell.
- 1 2. The method of claim 1, wherein said oligonucleotide
2 comprises a terminal phosphothiorate moiety and a phosphodiester backbone.
- 1 3. The method of claim 1, wherein said oligonucleotide passes
2 cell membranes and accumulates in the nuclear compartment of said cell.
- 1 4. The method of claim 1 wherein said cell is a cultured cell.
- 1 5. The method of claim 1, wherein said cell is selected from the
2 group consisting of an epithelial cell and an endothelial cell.
- 1 6. The method of claim 4, wherein said cell is selected from the
2 group consisting of renal cortical cell, renal fibroblast cell, hepatocyte, pancreatic
3 islet, renal interstitial cell, parathyroid cell, thyroid cell, pituitary cell, ovarian cell
4 and testicular cell.
- 1 7. The method of claim 1, wherein said cell is grown in two
2 dimensional culture.
- 1 8. The method of claim 1, wherein said shear stress response
2 element is selected from the group consisting of GAGACC and GGTCTC.
- 1 9. The method of claim 1, wherein the gene encodes a protein
2 selected from the group consisting of megalin, cubulin, erythropoietin and 1-a-
3 hydroxylase.
- 1 10. The method of claim 1, wherein the concentration of said
2 oligonucleotide is from about 10 nm to about 10 mm.

1 11. A transcription factor decoy, comprising an oligonucleotide
2 sequence directed against a nucleotide sequence encoding a shear stress response
3 element.

1 12. The transcription factor decoy of claim 11, wherein said
2 nucleotide sequence encoding a shear stress response element has a sequence
3 selected from the group consisting of GAGACC and GGTCTC.

1 13. A method of producing a functional protein, comprising the
2 steps of:
3 isolating mammalian cells;
4 placing said cells into a rotating wall vessel containing a cell culture
5 comprising culture media and culture matrix;
6 producing three-dimensional cell aggregates under simulated
7 microgravity conditions; and
8 detecting expression of the functional protein in the cell culture.

1 14. The method of claim 13, wherein said simulated microgravity
2 conditions comprise a balance between gravity and oppositely directed physical
3 forces.

1 15. The method of claim 14, wherein said physical forces are
2 selected from the group consisting of sedimentational shear stress, centrifugal
3 forces, viscosity and coriolus forces.

1 16. The method of claim 13, wherein said functional protein is
2 selected from the group consisting of a hormone, a toxin receptor and a shear stress
3 dependent functional biomolecule.

1 17. The method of claim 16, wherein said hormone is selected
2 from the group consisting of 1,25-dihydroxy-vitamin D3 and erythropoietin.

1 18. The method of claim 16, wherein said toxin receptor is
2 selected from the group consisting of megalin and cubulin.

1 19. The method of claim 16, wherein said shear stress dependent
2 functional biomolecule is selected from the group consisting of villin, magnesium
3 dependent superoxide dismutase, nitric oxide synthase, c-fos, c-jun, platelet derived
4 growth factor-b, transforming growth factor-b, tissue-type plasminogen activator
5 and monocyte chemotactic protein-1, megalin, cubulin, erythropoietin and 1-a-
6 hydroxylase.

1 20. The method of claim 13, wherein said cells are selected from
2 the group consisting of renal cortical cells, renal fibroblast cells, hepatocytes,
3 pancreatic islets, renal interstitial cells, parathyroid cells, thyroid cells, pituitary
4 cells, ovarian cells and testicular cells.

1 21. The method of claim 13, wherein said cell is selected from the
2 group consisting of epithelial cell and endothelial cell.

1 22. The method of claim 13, wherein said cell contains shear
2 stress response elements.

1 23. The method of claim 22, wherein said shear stress response
2 element is selected from the group consisting of GAGACC and GGTCTC.

1 24. The method of claim 13, wherein said rotating wall vessel is
2 initiated and maintained from about 6 rotations per minute to about 16 rotations per
3 minute.

1 25. The method of claim 15, wherein said sedimentational shear
2 stress is from about 0.2 dynes/cm² to about 1.0 dynes/cm².

1 26. The method of claim 13, wherein said culture matrix contains
2 a core structure selected from the group consisting of cell aggregates and
3 microcarrier beads.